## AMENDMENT TO THE CLAIMS

This listing of claims will replace all prior versions of claims in the application.

Listing of Claims:

1-5 (Cancelled)

6. (Currently Amended) A method for detecting an increased risk of developing ~~a neural tube defect,~~ Down's Syndrome~~, or~~ cardiovascular disease, or cancer in a mammalian embryo or fetus, said method comprising detecting the presence of a polymorphic methionine synthase reductase (MTRR) in a test subject, wherein said test subject is said embryo or fetus or a future parent of said embryo or said fetus, and wherein detection of a homozygous MTRR polymorphism in said future parent, said embryo, or said fetus, or detection of either a homozygous or heterozygous MTRR polymorphism in both future parents indicates an increased risk of developing said neural tube defect, Down's Syndrome, or cardiovascular disease in said embryo or said fetus, wherein said polymorphism comprises

~~(a)~~ a G instead of an A at position 66 relative to the first nucleotide of the start codon of MTRR~~;~~

~~(b) a G instead of an A at position 110 relative to the first nucleotide of the start codon of MTRR;~~

~~(c) a deletion of 4 nucleotides starting from position 1675 (nucleotides 1675-1678) relative to the first nucleotide of the start codon of MTRR, or~~

~~(d) a deletion of 3 nucleotides starting from nucleotide 1726 (nucleotides 1726-1728) relative to the first nucleotide of the start codon of MTRR.~~

7. (Original) The method of claim 6, wherein said polymorphic MTRR is detected by analyzing nucleic acid from said test subject.

8. (Original) The method of claim 7, wherein said nucleic acid is genomic DNA.

9. (Original) The method of claim 7, wherein said nucleic acid is cDNA.

10. (Cancelled)

11. (Original) The method of claim 7, said method further comprising:

a) PCR-amplifying a segment of MTRR nucleic acid using primers MSG108S (SEQ ID NO: 49) and AD292 (SEQ ID NO: 50), and

b) digesting the product of the PCR amplification reaction with the restriction enzyme *Nde* I, wherein a PCR product that is digested by *Nde* I indicates an increased risk of developing a neural tube defect in a mammalian embryo or fetus.

12. (Withdrawn) The method of claim 6, wherein said polymorphic MTRR is detected by analyzing MTRR polypeptide from said test subject.

13. (Original) The method of claim 6, wherein said test subject is a future female parent of said embryo or said fetus.

14. (Original) The method of claim 6, wherein said test subject is said embryo or said fetus.

15. (Withdrawn) The method of claim 6, said method further comprising detecting the presence of a polymorphic methylenetetrahydrofolate reductase (MTHFR) in a test subject, wherein detection of said polymorphic MTHFR indicates an increased risk of developing said neural tube defect, Down's Syndrome, or cardiovascular disease in said embryo or said fetus.

16. (Withdrawn) The method of claim 15, wherein said polymorphic MTHFR has a T instead of a C at a nucleotide position equivalent to position 677 of SEQ ID NO: 51.

17. (Withdrawn) The method of claim 15, wherein said polymorphic MTHFR is detected by analyzing nucleic acid from said test subject.

18. (Withdrawn) The method of claim 15, wherein said polymorphic MTHFR is detected by analyzing polypeptide from said test subject.

19. (Withdrawn) The method of claim 6, said method further comprising measuring the level of cobalamin in said test subject, wherein a low cobalamin level indicates an increased risk of developing said neural tube, cardiovascular disease or Down's Syndrome defect in said embryo or said fetus.

20. (Withdrawn) The method of claim 6, wherein said polymorphic MTRR contains a methionine instead of an isoleucine at amino acid position 22.

21. (Original) The method of claim 6, wherein said cardiovascular disease is premature coronary artery disease.

22-34 (Cancelled)

35. (Currently Amended) A method for detecting an increased risk of Down's Syndrome, ~~hyperhomocysteinemia,~~ cardiovascular disease, or cancer in a mammal, said method comprising detecting the presence of a homozygous MTRR polymorphism that indicates an increased risk of Down's Syndrome, ~~hyperhomocysteinemia,~~ cardiovascular disease, or cancer in said mammal, wherein said polymorphism comprises

~~(a)~~ a G instead of an A at position 66 relative to the first nucleotide of the start codon of MTRR~~;~~

~~(b) a G instead of an A at position 110 relative to the first nucleotide of the start codon of MTRR,~~

~~(c) a deletion of 4 nucleotides starting from position 1675 (nucleotides 1675-1678) relative to the first nucleotide of the start codon of MTRR, or~~

~~(d) a deletion of 3 nucleotides starting from nucleotide 1726 (nucleotides 1726-1728) relative to the first nucleotide of the start codon of MTRR~~.

36. (Previously Presented) The method of claim 6, wherein said test subject is human.

37. (Previously Presented) The method of claim 35, wherein said mammal is human.

38. (Previously Presented) The method of claim 6, further comprising measuring the level of cobalamin in said test subject.

39. (Previously Presented) The method of claim 35, further comprising measuring the level of cobalamin in said mammal.

40-41 (Cancelled)

42. (Currently Amended) The method of claim 35, wherein said polymorphic MTRR is detected by analyzing nucleic acid from said mammal ~~test subject~~.

43. (Previously Presented) The method of claim 35, wherein said cardiovascular disease is premature coronary artery disease.

44. (New) The method of claim 6 or 35, wherein said cancer is colon cancer.

45. (New) A method for detecting an increased risk of a folate/cobalamin metabolic disorder in a mammal, said method comprising detecting the presence of a homozygous MTRR polymorphism that indicates an increased risk of a folate/cobalamin metabolic disorder in said mammal, wherein said polymorphism comprises

(a) a G instead of an A at position 66 relative to the first nucleotide of the start codon of MTRR,

(b) a deletion of 4 nucleotides starting from position 1675 (nucleotides 1675-1678) relative to the first nucleotide of the start codon of MTRR, or

(c) a deletion of 3 nucleotides starting from nucleotide 1726 (nucleotides 1726-1728) relative to the first nucleotide of the start codon of MTRR.

46. (New) The method of claim 45, wherein said folate/cobalamin metabolic disorder is megablastic anemia, developmental delay, hyperhomocysteinuria, or hypomethionemia.

47. (New) The method of claim 45, wherein said mammal is human.

48. (New) The method of claim 45, further comprising measuring the level of cobalamin in said mammal.

49. (New) The method of claim 45, wherein said polymorphic MTRR is detected by analyzing nucleic acid from said mammal.

50. (New) A method for detecting an increased risk of developing a neural tube defect in a mammalian embryo or fetus, said method comprising detecting the presence of a polymorphic methionine synthase reductase (MTRR) and low serum cobalamin level in a test subject, wherein said test subject is said embryo or fetus or a future parent of said embryo or said fetus, and wherein detection of a homozygous MTRR polymorphism in said future parent, said embryo, or said fetus, or detection of either a homozygous or heterozygous MTRR polymorphism in both future parents indicates an increased risk of developing said neural tube defect in said embryo or said fetus, wherein said polymorphism comprises a G instead of an A at position 66 relative to the first nucleotide of the start codon of MTRR.

51. (New) The method of claim 50, wherein said test subject is human.

52. (New) The method of claim 50, wherein said polymorphic MTRR is detected by analyzing nucleic acid from said test subject.

53. (New) The method of claim 50, wherein said neural tube defect is spina bifida.

54. (New) The method of claim 50, wherein detecting said low serum cobalamin level comprises detecting a concentration of serum cobalamin that is less than 328 pmol/L in said fetus or embryo, or a concentration of serum cobalamin that is less than 259 pmol/L in said future parent of said embryo or fetus.